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EXAMINER	
HELM, CARALYNNE E	

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1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,673	BROGMANN ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-19 and 24-54* is/are pending in the application.

4a) Of the above claim(s) *27-40 and 50-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12-19,24-26 and 41-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/9/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

To summarize the current election, applicant elected Group I and the species containing an opioid analgesic salt and an opioid antagonist salt are present where alkaline or water-swellable substances as well as acrylic acid and/or hydroxyalkylcelluloses are absent.

Claims 27-40 and 50-54 were withdrawn from further consideration pursuant to 37 CFR 1.14239b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Terminal Disclaimer

The terminal disclaimer does not comply with 37 CFR 1.321(b) and/or (c) because: 37 CFR 1.321 (c)(3) requires that a terminal disclaimer, "[i]nclude a provision that any patent granted on that application or any patent subject to the reexamination proceeding shall be enforceable only for and during such period that said patent is commonly owned with the application or patent which formed the basis for the judicially created double patenting." The words "legal title" do not include common ownership as to equitable title.

NEW REJECTIONS

Claim Objections

Claim 1 is objected to because of the following informalities: it appears that "naloxonazinene" is a misspelling of naloxonazine since no chemical structure was able to be found for the recited compound. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 12-19, 24-26, and 41-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There was no description of the claimed pharmaceutical as a plurality of formulations in the disclosure as filed. Therefore this recitation in the claims constitutes new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 12-19, 24-26, and 41-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear what applicants intend by the recitation "a plurality to storage stable pharmaceutical formulations." This recitation appears to require a collection of compositions, but it is not clear if this requires a single preparation that is composed of a set of formulations that may or may not be composed of same components or if the recitation is simply a genus of formulations. For the sake of application of prior art, the recitation is interpreted a genus of formulations.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquiries of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10, 12-19, 24-26, and 41-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (previously cited) in view of Gordon et al. (US Patent No. 4,457,933) and Oshlack et al. (previously cited).

Miller et al. teach an oral controlled (sustained) release composition that releases the hydrochloride salt of the opioid analgesic tramadol (see abstract and page 2 lines 6-18; instant claims 1, 12, 17, and 24). Miller et al. also teaches an uncoated tablet with tramadol hydrochloride, ethyl cellulose, lactose, cetostearyl alcohol (also known as cetylstearyl alcohol), magnesium stearate, and purified talc (see page 7 example 1; instant claims 1-8, 16-17, 41, 42, and 44). In addition, a coating is taught to be present only if desired, indicating that Miller et al. envisioned uncoated as well as coated tablet formulations (see page 5 lines 30). Further, Miller et al. teach the inclusion of additional

components in the tablet composition including diluents, lubricants, binders and glidants, particularly exemplifying dibutyl sebacate as one particular other ingredient (see page 4 lines 48-50; instant claim 9). Additionally, Miller et al. teach that the composition contains at least one long chain hydrocarbon (e.g. cetostearyl alcohol) and that these compounds can be fatty acids as well as fatty alcohols (see page 4 lines 32-33). In particular, Miller et al. teach these hydrocarbons to be C_{12}-C_{40}, which includes stearic acid (see page 4 lines 32-33; instant claim 43). In light of these teachings, it would have been obvious to one of ordinary skill in the art at the time invention was made to have included stearic acid in the taught composition. Furthermore, production of particular release kinetics based upon the proportions and arrangement of constituents would be known to one of ordinary skill in the art. The Miller et al. reference specifically teaches the varying amounts of the matrix components (see page 4 lines 41-47), thus at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize such parameters as a matter of routine experimentation. Miller et al. do not specifically teach the inclusion of an opioid antagonist in their taught composition nor do they address the stability of the composition over a two year period.

Gordon et al. teach the combination of an opioid analgesic and antagonist in an oral composition to provide pain relief and reduce the potential addiction a well as provide a deterrent to parenteral abuse of the product (see column 2 lines 5-14; instant claims 1 and 24). The opioid to opioid antagonist ratio is taught to be 3.5:1 where naloxone is present at 1 to 3 mg, which corresponds to an oxycodone level of 1 to 10.5

mg (see column 3 lines 19-25; instant claims 13-15, 25-26, 45-46, and 48-49). In addition, Gordon et al. also teach the administration of the hydrochloride salt of naloxone and oxycodone in the course of testing for their analgesic-antagonist combinations (see table 1 and column 5 lines 45-46; instant claims 4 and 44)

Oshlack et al. teach a composition similar to that of Miller et al. where ethyl cellulose is combined with stearyl alcohol along with other claimed excipients and a tramadol hydrochloride salt (see table 1). Oshlack et al. stress the importance of storage stability of dosage forms (see column 1 lines 18-20). Oshlack et al. teach a means by which their composition would be able to be stored at 25°C with 60% humidity for two years and maintain its stability (see column 17 lines 19-37 and column 18 lines 43-49; instant claim 10). Thus it was known at the time of the invention how to obtain the claimed stability characteristics for the product taught by Miller et al.

Since both Miller et al. and Gordon et al. teach a sustained release oral opioid composition, it would have been obvious to one of ordinary skill in the art at the time of the invention exchange an oxycodone salt for the tramadol salt in Miller et al. as a functionally equivalent opioid analgesic. Given the additional teachings of Gordon et al. that such compounds are prone to abuse, it would have also been obvious to include naloxone in this composition at the ratios and amounts taught by Gordon et al. There would have been a reasonable expectation of success for this combination to one of ordinary skill in the art to at the time of the invention. In addition, the inclusion of the hydrochloride forms of oxycodone and naloxone would also have been obvious since both were known to be functionally equivalent, pharmaceutically active forms of

oxycodone and naloxone, respectively (see instant claims 4, 12, and 44).Furthermore, given the teachings of Oshlack et al. that storage stability was important for dosage forms and known methodologies for achieving storage stable, solid opioid analgesic dosage forms composed of ethyl cellulose like those taught by Miller et al., it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a product that could be stored for at least two years at the recited "standard conditions".

Instant claims 18-19 and 47 are product by process claims whose processes provide no additional patentable structure to the claimed product. According to MPEP 2113 " '[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.' In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)". Therefore since the claimed components and those of Miller et al. in view of Gordon et al. and Oshlack et al are the same, the product taught by this modified Miller et al. reference meet the limitations of these product-by-process claims.

Finally, the limitations of the matrix being a diffusion matrix that is substantially non-erosive, substantially non-swellable, as well as releases the compounds in an invariant and independent manner are viewed as properties of the composition based upon its constituent materials. Thus since Miller et al. in view of Gordon et al. and

Oshlack et al. teach the same composition as that claimed, this composition would function in the same manner and have the same properties. It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe necessarily includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph). Therefore claims 1-10, 12-19, 24-26, and 41-49 are obvious over Miller et al. in view of Gordon et al. and Oshlack et al.

Claims 1-8, 10, 12-19, 24-26, and 41-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oshlack et al. (US Patent No. 5,958,452 – henceforth Oshlack B) in view of Gordon et al. and Oshlack et al. (US Patent No. 5,681,585 – henceforth Oshlack C), Odds et al. (US Patent No. 6,207,142), and Grimm (Drug Development and Industrial Pharmacy 1998 24:313-324).

Oshlack B teaches oral sustained release opioid pharmaceutical formulations (see column 1 lines 10-12 and column 3 lines 40-43; instant claims 1 and 24). In particular, a listing of preferred opioid compounds is taught along with their pharmaceutically acceptable salts (see column 7 lines 9-39; instant claims 1 and 12). Within this set, oxycodone is taught as preferred variety (see column 7 lines 35-39; instant claim 1). An exemplified tablet preparation is taught to include an opioid analgesic salt, ethyl cellulose, tributyl citrate, stearyl alcohol, talc and magnesium

stearate (see example 28; instant claims 1-8, 16-17, 41-42, and 44). Oshlack B also teaches the inclusion of stearic acid as a retardant to control the release of active when exposed to aqueous solutions (see column 4 lines 11-16 and 21-25; instant claim 43). Oshlack B does not explicitly teach the presence of an antagonist, particular oxycodone salts, or stability of the preparation.

Gordon et al. teach the combination of an opioid analgesic and antagonist in an oral composition to provide pain relief and reduce the potential addiction a well as provide a deterrent to parenteral abuse of the product (see column 2 lines 5-14; instant claims 1 and 24). The opioid to opioid antagonist ratio is taught to be 3.5:1 where naloxone is present at 1 to 3 mg, which corresponds to an oxycodone level of 1 to 10.5 mg (see column 3 lines 19-25; instant claims 13-15, 25-26, 45-46, and 48-49). Gordon et al. teaches starch in addition to lactose and talc as suitable carriers for such compositions (see column 4 lines 12-15; instant claim 6). In addition, Gordon et al. also teach the administration of the hydrochloride salt of naloxone and oxycodone in the course of testing for their analgesic-antagonist combinations (see table 1 and column 5 lines 45-46; instant claims 4 and 44).

Oshlack C teaches stabilized controlled release pharmaceutical dosage forms as well as stress the importance of this property in dosage forms (see title and column 1 lines 29-34). Their exemplified dosage forms are ethyl cellulose containing opioid preparations (see example 1). Oshlack C teaches a means by which to stabilize such compositions for extended storage (see column 3 lines 26-30 and 42-52). One of ordinary skill in the art would desire long term storage stability in order to have product

consistency in spite of the time lapse between production and use by the customer (e.g. due to shipping, distribution, etc.). While Oshlack C is silent as to the desired duration of storage stability, Odds et al. teach that two years at standard room conditions is well recognized by government regulatory agencies in the pharmaceutical field as an acceptable duration fro storage stability (see column 4 line 63-column 5 line 1). Grimm teaches that such standard conditions for the United States is 25ºC and 60% humidity (see abstract; instant claim 10). Thus it was known at the time of the invention how to obtain the claimed stability characteristics for the product taught by Oshlack B in view of Gordon et al.

Given the teachings of Gordon et al. that oxycodone compositions are prone to abuse, it would have also been obvious to one of ordinary skill in the art at the time of the invention to include naloxone in this composition at the ratios and amounts taught by Gordon et al. There would have been a reasonable expectation of success for this combination to one of ordinary skill in the art to at the time of the invention. In addition, the inclusion of the hydrochloride forms of oxycodone and naloxone would also have been obvious since both were known to be functionally equivalent, pharmaceutically active forms of oxycodone and naloxone, respectively (see instant claims 4, 12, and 44). Additionally, inclusion of starch as a carrier along with the talc, would have been obvious as well given their functional equivalence (e.g. in re Kerkhoven). Furthermore, giving the teachings of Oshlack C, Odds et al., and Grimm that storage stability was important for dosage forms and known methodologies for achieving storage stable, solid opioid analgesic dosage forms composed of ethyl cellulose, it would have been obvious

to one of ordinary skill in the art at the time the invention was made to produce a product that could be stored for at least two years at the recited "standard conditions".

Instant claims 18-19 and 47 are product by process claims whose processes provide no additional patentable structure to the claimed product. According to MPEP 2113 " '[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.' In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)". Therefore since the claimed components and those of Oshlack B in view of Gordon et al., Oshlack C, Odds et al., and Grimm are the same, the product taught by this modified Miller et al. reference meet the limitations of these product-by-process claims.

Finally, the limitations of the matrix being a diffusion matrix that is substantially non-erosive, substantially non-swellable, as well as releases the compounds in an invariant and independent manner are viewed as properties of the composition based upon its constituent materials. Thus since Oshlack B in view of Gordon et al., Oshlack C, Odds et al., and Grimm teach the same composition as that claimed, this composition would function in the same manner and have the same properties. It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe necessarily includes functions that are newly cited or is identical to a product

instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph). Therefore claims 1-8, 10, 12-19, 24-26, and 41-49 are obvious over Oshlack B in view of Gordon et al., Oshlack C, Odds et al., and Grimm.

Claims 1-5 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oshlack B in view of Gordon et al., Oshlack C, Odds et al., and Grimm as applied to claims 1-8, 10, 12-19, 24-26, and 41-49 above, and further in view of Chasin et al. (US Patent No. 6,103,261).

Oshlack B in view of Gordon et al., Oshlack C, Odds et al., and Grimm make obvious the composition of claims 1-5. While triethyl citrate is taught present in this preparation, dibutyl sebacate is not explicitly taught.

Chasin et al. teach opioid oral compositions like those of Oshlack B in view of Gordon et al., Oshlack C, Odds et al., and Grimm (see abstract). Specifically, Chasin et al., teach plasticizers in these compositions that include triethyl citrate and dibutyl stearate (see column 6 lines 43-45).

As functionally equivalent plasticizers intended for the use in the same type of composition, it would have been obvious to one of ordinary skill in the art at the time of the invention to exchange dibutyl sebacate for the triethyl citrate taught by Oshlack B in view of Gordon et al., Oshlack C, Odds et al., and Grimm. Therefore claims 1-5 and 9

are obvious over Oshlack B in view of Gordon et al., Oshlack C, Odds et al., Grimm, and Chasin et al.

Response to Arguments

Applicant's arguments (e.g. regarding claim amendments and cited references in view of 35 USC 103(c)) and exhibits filed November 9, 2009 have been fully considered and are persuasive. New grounds of rejection are presented over new combinations of references.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The rejections and/or objections detailed above are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615